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NOVEL COMPOSITION

Field of the invention

The present invention relates to a pMDI formulation of formoterol in a blend of propellants for use in the treatment of inflammatory conditions/disorders, especially respiratory diseases such as asthma, COPD and rhinitis.

Background of the invention

Stability is one of the most important factors which determines whether a compound or a mixture of compounds can be developed into a therapeutically useful pharmaceutical product.

Formoterol is known in the art, and is marketed as Oxis® in a dry powder inhaler. There are a variety of other inhalers by which a respiratory product can be administered, such as pressurised metered dose inhalers (pMDI's). Formulations for pMDI's may require certain excipients such as those disclosed in WO 93/05765. It is also known that drug deposition can be reduced by internally coating the cans of pMDI's.

It has now been found that certain HFA formulations comprising formoterol together with polyvinylpyrrolidone (PVP) and polyethylene glycol (PEG) exhibit excellent product stability when contained in pMDI's having internally coated cans and where the pMDI's are wrapped to exclude moisture.

Description of the invention

In accordance with the present invention, there is provided a pharmaceutical composition suitable for use in a pMDI having a coated can fitted with a retention valve, the pMDI being packaged in a moisture resistant wrapping, comprising formoterol, HFA 227, HFA 134a, PVP and PEG.

Preferably the PVP is present from about 0.0001 to about 0.01 %w/w and the PEG is present from about 0.001 to about 0.15% w/w.

Preferably the PVP is present in an amount of 0.001 % w/w. Preferably the PVP is PVP K25.

Preferably the PEG is present in an amount of 0.1 % w/w. Preferably the PEG is PEG 1000.

The HFA 134a nd HFA 227 can be present in any suitable ratio. Preferably the HFA 134a and HFA 227 are present in a ratio of 75% to 25%.

Preferably the can is coated and fitted with a retention valve. Suitable coatings include PFA polymers known in the art which can be applied using known techniques. Suitable retention valves include Valois RCS valves

Preferably the pMDI is packaged in a moisture resistant wrapping such as a foil pouch optionally containing a dessicant.

Preferably the concentrations of formoterol is such that the formulation delivers formoterol at 4.5 mcg per actuation.

The formoterol can be in the form of a mixture of enantiomers. Preferably the formoterol is in the form of a single enantiomer, preferably the R;R enantiomer. The formoterol can be in the form of the free base, salt or solvate, or a solvate of a salt, preferably the formoterol is in the form of its fumarate dihydrate salt. Other suitable physiologically salts that can be used include chloride, bromide, sulphate, phosphate, maleate, tartrate, citrate, benzoate, 4-methoxybenzoate, 2- or 4-hydroxybenzoate, 4-chlorobenzoate, p-toluenesulphonate, benzenesulphonate, ascorbate, acetate, succinate, lactate, glutarate, gluconate, tricaballate, hydroxynapaphthalenecarboxylate or oleate.

The pharmaceutical compositions according to the invention can be used for the treatment or prophylaxis of a respiratory disorder, in particular the treatment or prophylaxis of asthma, rhinitis or COPD.

In a further aspect the invention provides a method of treating a respiratory disorder, in particular asthma, rhinitis or COPD, in a mammal which comprises administering to a patient a pharmaceutical composition as herein defined.

The compositions of the invention can be inhaled from any suitable MDI device. Doses will be dependent on the severity of the disease and the type of patient, but are preferably 4.5 mcg per actuation as defined above.

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Experimental section

The compositions may be produced by cold fill or pressure fill techniques. In cold filling, the ingredients are placed in a cooled mixing vessel, cooled liquefied propellant added and a dispersion produced by vigorous stirring. Alternatively, a slurry may be prepared of the ingredients in a portion of cooled liquid propellant and the remainder of the liquefied propellant added under vigorous stirring. Aliquots of the dispersed composition are then filled into cooled aerosol cans and sealed with a suitable valve, e.g. a metering valve.

In pressure filling, the ingredients are placed in a pressure vessel, liquefied propellant added under pressure through a valve and a dispersion of the ingredients in the liquefied dispersed composition are then filled, under pressure, through the valve into suitable cans provided with appropriate valves, e.g. metering valves.

Claims.

1. A pharmaceutical composition suitable for use in a pMDI having a coated can fitted with a retention valve, the pMDI being packaged in a moisture resistant wrapping,.comprising formoterol, HFA 227, HFA 134a, PVP and PEG.

2. A pharmaceutical composition according to claim 1 in which the PVP is present from about 0.0001 to about 0.01 %w/w and the PEG is present from about 0.001 to about 0.15% w/w

3. A pharmaceutical composition according to claim 1 in which the PVP is PVP K25.

4. A pharmaceutical composition according to claim 1 or 2 in which the PVP is present in an amount of 0.001% w/w.

5. A pharmaceutical composition according to any one of claims 1 to 3 in which the PEG is PEG 1000.

6. A pharmaceutical composition according to any one of claims 1 to 4 in which the PEG is present in an amount of 0.1% w/w.

7. A pharmaceutical composition according to any one of claims 1 to 5 in which formoterol is in the form of its fumarate dihydrate salt

8. A pharmaceutical composition according to any one of claims 1 to 6 in which the formoterol is in the form of the single R,R-enantiomer.

9. A pharmaceutical composition according to any one of claims 1 to 7 in which the ratio of HFA 134a to HFA227 is 75% to 25%.

10. A pharmaceutical composition according to any one of claims 1 to 8 for use for the treatment or prophylaxis of a respiratory disorder.

11. A phairmaceutical composition according to any one of claims 1 to 9 for use for the treatment or prophylaxis of asthma, rhinitis or COPD.

12. A method of treating a respiratory disorder in a mammal which comprises administering to a patient a pharmaceutical composition according to any one of claims 1 to 9.

Abstract

The invention relates to novel pharmaceutical composition useful in the treatment of respiratory disorders such as asthma, rhinitis and chronic obstructive pulmonary disease (COPD).